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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/650,608 | 08/28/2003 | Jean-Pol Cassart | B45300-1 | 8978 |

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| EXAMINER | |
|---|---|
| DAVIS, MINH TAM B | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 03/05/2008 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/650,608 | CASSART ET AL. | |
| | Examiner | Art Unit | |
| | MINH-TAM DAVIS | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *7-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***DETAILED ACTION***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/11/08 has been entered.

**Claims 7-9 are examined in the instant application.**

***Claim Rejections - 35 USC § 112, First Paragraph, Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-9 remain rejected under 35 U.S.C. 112, first paragraph, because the specification and the claims lack enablement for a method for inducing an immune response to SEQ ID NO:2 in a human, or non-human animal, using a peptide fragment of SEQ ID NO:2, i.e. SEQ ID NO:25, for reasons already of record in paper of 09/10/07.

The response asserts that the rejection should be withdrawn for two (2) main reasons.

**Reason (1)** The rejection construes the claims as if they recite an endpoint of tumor reduction. None of the claims group currently under examination by the Office recited "treating cancer," "cancer treatment," "tumor reduction," or the like, nor do any of the currently pending claims recite "treating cancer," "cancer treatment," "tumor reduction," or the like. Contrary to

MPEP § 2107.02, the Office Action is reading into the claim limitations that are not there. Thus, the rejection should be withdrawn because it is based the legally unsupportable construction that the claims require a step of successfully treating cancer or reducing tumor size.

The response has been considered but is not found to be persuasive for the following reasons:

The claims are **reasonably interpreted** as a method for **treating cancer**, such as reduction of cancer cell growth in vivo, as contemplated in the specification, via inducing an immune response. The specification contemplates testing the effect of the stimulated T cells on tumor cells transfected with cDNA encoding SEQ ID NO:2 (p.64, last two paragraphs, bridging p.65).

The encompassed method for treating cancer is not enabled, because of the unpredictability of cancer treatment, including cancer treatment using a CTL epitope, in view of the teaching of Kirkin et al, Boon, Gaiger et al, Ezzell et al, and Spitler et al, all of record.

The claims also encompass a method for **inducing an immune response in** a human or non-human animal having **cancer**, as contemplated in the specification.

One cannot predict that the claimed method would induce sufficient CTL response or production of an antibody to SEQ ID NO:2 in a cancer patient, using a fragment of SEQ ID NO:2 comprising the peptide SEQ ID NO:25, because of the well known immunosuppression and immune tolerance in cancer, in view of the teaching of Smith et al, and White al, Boon, all of record.

The specification however does not have any objective evidence of successful treatment of cancer by CTLs or antibodies induced by administration of the peptide comprising SEQ ID

NO: 25. The specification does not have objective evidence that sufficient and high affinity CTLs or antibodies are produced in cancer patients with cancer burden, where the problem of cancer tolerance, with suppression of CTLs and/or antibody production, is common. The specification only discloses that a peptide fragment comprising SEQID NO:25 **in vitro** activates T cells from PBMC of 3 **healthy** donors, which T cells recognize DCs pulsed with full length SEQ ID NO:2 (Example 10, on pages 68-71).

The response asserts that the Action erroneously states that "[t]he claims do not recite the use of adjuvants with SEQ ID NO:25 .... " . The response asserts that claim 9 recites adjuvants. The response requests that claim 9 be reviewed because it expressly recites adjuvants.

The response has been considered but is not found to be persuasive for the following reasons:

Except claim 9, none of other claims recite the use of adjuvants with a peptide fragment of SEQ ID NO:2, comprising SEQ ID NO:25.

Concerning claim 9, there is no evidence that the claimed peptide has a synergistic effect on the added adjuvants, concerning cancer treatment.

The response recites the following second reason:

**Reason (2)** The improper claim construction allows the enablement analysis to overlook bona fide uses for Applicants' claimed method for inducing an immunoresponse. Applicants have disclosed that their methods can be used "to generate antibodies or reagents specific for the polypeptide of the present invention, as diagnostic reagents to detect...genetic or biochemical

markers in blood or tissues that will enable the detection of very early changes along the carcinogenesis pathway will help in determining the best treatment for the patient." See paragraphs [0182]-[183]. Those of skill in the art understand that such "surrogate tumor markers" can be used to diagnose and stage different forms and states of cancer. See paragraph [0183]. For example, one could easily use these markers to compare the expression of a particular gene between a diseased tissue and a normal tissue. See paragraph [0184]. The comparison can be made at the protein level. See paragraph [0188]. Those of skill in the art can also easily detect tumor marker expression levels and subcellular localization by using antibodies to the corresponding protein. See paragraph [0200]. Antibodies for use in the method are easy to make and can be obtained by administering the polypeptides or epitope-bearing fragments to an animal, which may be a non-human animal, using routine protocols. However, these uses have received no examination due to the Office Action's improper claim construction.

The response has been considered but is not found to be persuasive for the following reasons:

Applicant's argues limitation not in the claims. The claims are not drawn to a method for diagnosis of cancer, by inducing an immune response.

The response asserts that White does not provide any evidence that the relevant antigen of the present claims, i.e., HASH2 (SEQ ID NO:2) is either internalized or down-regulated. The response asserts that consequently, the Examiner was invited to provide some reference to support such a premise or to provide an affidavit pursuant to 37 CFR 1.104(d)(2) if the premise

is based upon personal knowledge. The response asserts that none has been forth coming and this point of the rejection therefore cannot be relied upon by the Office.

The response has been considered but is not found to be persuasive for the following reasons:

In view of the teaching of White et al, one cannot predict the behavior of an antigen, unless tested. One cannot predict that the claimed antigen is not internalized or downregulated in cancer cells, in view of the teaching of White et al..

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
February 19, 2008
/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643